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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/766,412	01/22/2001	Ruowen Ge	1781-0215P	7335

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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/766,412	GE ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,13-16,19,20,22,23 and 25-28* is/are pending in the application.

4a) Of the above claim(s) *3-5,9,10,15,16,20 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-8,13,14,19,22 and 25-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2,7*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT OF IDS, RESPONSE TO RESTRICTION REQUIREMENT, STATUS OF THE APPLICATION AND CLAIMS

1. The information disclosure statement (IDS) and Form PTO-1449 filed 1/22/01 and 1/25/02 and the response to the restriction requirement filed 3/22/04 are acknowledged, entered and considered. Claims 1-10, 13-16, 19, 20, 22, 23 and 25-28 are now pending in the application of which claims 3-5, 9, 10, 15, 16, 20 and 23 are withdrawn from consideration as non-elected invention.

ELECTION WITH TRAVERSE

2. Applicant's election with traverse of Group II (drawn to endostatin derivatives) in Paper No. 12 is acknowledged. The traversal is on the ground(s) that the inventions of Groups I-IV as disclosed and claimed in this application would most efficiently be examined together herein is unpersuasive. Groups I-IV are unrelated and are different inventions having independent compounds/compositions, which are not connected in design, operation or effect. Although, the compositions/compounds of Groups I-IV are used as pharmaceutical formulations for the same method of preventing or treating primary tumor growth or metastasis by preventing undesired angiogenesis, however, the compositions/compounds have different sources, structures resulting in different functions and different effect. The groups require different patent and literature search, and a reference teaching the use of plasminogen which is a plasma glycoprotein synthesized in the liver (See e.g. page 1, last paragraph in the instant specification) as

claimed in Group I will not teach Groups II-IV proteins. Further, the proteins of Groups II-IV, each differs in source and structure, wherein the endostatin protein of Group II is identified from a hemangioendothelioma cell line having a 20 kDa C-terminal fragment of collagen XVIII (See e.g., page 2, lines 21-25 in the instant specification), Group III VEGF protein is a potent endothelial specific mitogen (See page 3, lines 1-3 in the instant specification) and Group IV KDR/FLK-1 receptor proteins are expressed in endothelial cells and stimulate endothelial cell proliferation and migration (See e.g., page 2, lines 5-8 in the instant specification). Thus, the compounds/compositions as grouped are independent and distinct inventions, which differ, in material make up and composition requiring different reaction conditions. Hence, one does not require the other for ultimate use and as such is capable of separate manufacture, use and sale, and is novel and patentable over each other.

Further, Applicant asserts that claims 9, 10, 15, 16, 20 and 23 were not restricted out or designated as being withdrawn from consideration by the Examiner, it is presumed that claims 9, 10, 15, 16, 20 and 23 will be examined along with the invention of Group II. Contrary to Applicant's assertion, Applicant has elected SEQ ID NO:30 with traverse on page 8, second paragraph of the remarks filed 9/25/03 (Paper No. 10). The Examiner has clearly indicated on pages 2-4 of election/restriction mailed 2/20/04 (Paper No. 11) that the sequences are patentably distinct because they are unrelated sequences and each unrelated sequence is considered a separate and distinct product, therefore, a further restriction is applied to each sequences. Thus, all SEQ ID NO's other than SEQ ID NO:30 are withdrawn from further consideration pursuant to 37 CFR

1.142(b) as being drawn to nonelected invention, there being no allowable generic or linking claim. Hence, the previous election/restriction has been modified on the merits of pending claims 1-8, 13, 14, 19, 22 and 25-28, as they read on elected SEQ ID NO:30, follows.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-8, 13, 14, 19, 22 and 25-28, drawn to plasminogen, pharmaceutical composition thereof and to a method for preventing or treating primary tumor growth or metastasis by preventing undesired angiogenesis, classified in classes 530 and 514, subclasses 380, 326, 2 and 13, respectively.

II. Claims 1-8, 13, 14, 19, 22 and 25-28, drawn to endostatin, pharmaceutical composition thereof and to a method for preventing or treating primary tumor growth or metastasis by preventing undesired angiogenesis, classified in classes 530 and 514, subclasses 311, 356, 326 and 13, respectively.

III. Claims 1-8, 13, 14, 19, 22 and 25-28, drawn to vascular endothelial growth factor (VEGF), pharmaceutical composition thereof and to a method for preventing or treating primary tumor growth or metastasis by

preventing undesired angiogenesis, classified in classes 530 and 514, subclasses 326, 399 and 13, respectively.

IV. Claims 1-8, 13, 14, 19, 22 and 25-28, drawn to KDR/FLK-1 receptor protein, pharmaceutical composition thereof and to a method for preventing or treating primary tumor growth or metastasis by preventing undesired angiogenesis, classified in classes 530 and 514, subclasses 326, 324 and 13, respectively.

Thus, clearly showing that all other sequences disclosed in claims 9 and 10 and dependent claims thereof (i.e., claims 15, 16, 20 and 23) are withdrawn from consideration as non-elected invention except for claims reading on SEQ ID NO:30.

Further, the Examiner regrets for the typographical errors in grouping claims 3-5 in Groups II-IV because claims 3-5 are drawn to plasminogen of Group I. Thus, Groups II-IV are hereby corrected each to comprise claims 1, 2, 6-8, 13, 14, 19, 22, and 25-28. Therefore, claims 3-5, 9, 10, 15, 16, 20 and 23 are withdrawn as non-elected invention for the reasons discussed above; hence, the Office action is directed to the merits of claims 1, 2, 6-8, 13, 14, 19, 22 and 25-28 as *per* elected invention.

Applicant is advised to cancel the non-elected invention.

OBJECTION TO THE SPECIFICATION

3. The disclosure is objected to because of the following informalities: on pages 6 and 7 recites "SEQ. ID. NOs.:....." and on page 9 recites "(SEQ. ID. Nos.....)". It is suggested according to USPTO practice that Applicant amends the specification by changing "SEQ. ID. NOs...." or SEQ. ID. Nos...." to "SEQ ID NOS:..." . Appropriate correction is required.

CLAIMS REJECTION-35 U.S.C. 112, 1st PARAGRAPH

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19, 22, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no description in the instant specification for the claimed methods of **preventing or treating a subject** for the conditions being claimed, such as undesired angiogenesis (claims 19 and 27) or primary tumor growth or metastasis by preventing undesired angiogenesis (claims 22 and 28). The specification demonstrates *in vitro* tests of bovine aorta endothelial cell (BAE) proliferation assay for their ability to inhibit BAE cell proliferation, which provides

a method for determining the anti-angiogenic activity of the peptides (See e.g., Examples 1-3 of the specification). Example 4 demonstrates that angio-3 can inhibit endothelial cell proliferation and retard tumor growth in mice. However, there is no *in vivo* showing for the effectiveness of the peptides as claimed nor there is a recognized model (identified as useful) being treated according to methods of **preventing or treating a subject** for the conditions being claimed.

CLAIMS REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

5. Claims 19, 22, 27 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19, 22, 27 and 28 are indefinite in the recitation "undesired angiogenesis" because it is not clear what the term "undesired angiogenesis" reflects since it is not defined in the specification nor in the claims, and as such renders the claims indefinite as to the condition being treated, other than being related to treating a tumor. Appropriate clarification is required.

CLAIMS REJECTION-35 U.S.C. § 102(b)

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6-8, 13, 14, 25 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by O'Reilly et al. (Cell, Vol. 88, pp. 277-285, January 24 1997).

O'Reilly et al. on page 277, right column, disclose endostatin peptide, which is a specific inhibitor of endothelial proliferation and is a potent angiogenesis inhibitor with a pharmaceutical formulations tested at doses of up to 100 mg/kg which overlaps with the unit dose of 20 μg/kg/day to 2 mg/kg/day of claims 14 and meet the limitations of pharmaceutical compositions of claims 13 and 26. Reference Figure 2 discloses a portion of endostatin peptide having 1-20 amino acid residues without any cysteine residues and therefore does not form disulfide bonds as directed to claims 1 and 6-8. Also, in Figure 2, the prior art discloses SEQ ID NO:30 (i.e., residues 7-19 which are QPVLHLVALNTPL) as directed to claim 25. On page 279, last paragraph and Figure 3, the reference shows an assay, which exhibits inhibition of angiogenesis in a chick chorioallantoic membrane (CAM) at doses of 10-20 μg/disc, which overlaps, with the dose of 10-25 μg/coverslip of claim 2. The reference teaches the identical compound/composition and would therefore be expected to have the identical properties and functions(s).

CONCLUSION AND FUTURE CORRESPONDENCE

7. Claims 1, 2, 6-8, 13, 14, 19, 22 and 25-28 are rejected and claims 3-5, 9, 10, 15, 16, 20 and 23 are withdrawn as non-elected invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272-0955. The examiner can normally be reached on Monday through Friday from 5:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306 for regular communications and (703) 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

AAM Mohamed/AAM

May 28, 2004